Claims

1. A method for reducing the level of Aβ secreted from a brain cell comprising contacting a mammalian brain cell with an agent that reduces expression or activity of a liver X receptor (LXR) protein.

2. The method of claim 1, wherein the agent is an agent that reduces LXR protein activity.

3. The method of claim 2, wherein the agent binds to the LXR protein.

4. The method of claim 3, wherein the agent is an antibody or an antibody fragment containing an antigen binding domain that binds to LXR protein.

5. The method of claim 2, wherein the agent is an antagonist of LXR function.

6. The method of claim 5, wherein the LXR antagonist is geranylgeranyl pyrophosphate (GGPP).

7. The method of claim 1, wherein the agent is an agent that reduces LXR protein expression.

8. The method of claim 7, wherein the agent is a molecule that induces RNA inhibition (RNAi).

9. The method of claim 7, wherein the agent is an antisense oligonucleotide.

10. The method of claim 7, wherein the agent reduces oxysterol and/or retinoic acid levels in the brain cell.

11. The method of claim 10, wherein the agent reduces oxysterol levels is a statin compound.

12. The method of claim 11, wherein the agent that reduces oxysterol levels is an inhibitor of a cytochrome P450 enzyme that generates oxysterols.

13. The method of claim 12, wherein the cytochrome P450 enzyme is CYP46 that makes 24-hydroxycholesterol.

14. The method of claim 7, wherein the agent is PPARδ modulator.

15. The method of claim 1, wherein said contacting occurs in vitro.

16. The method of claim 1, wherein the brain cell is a neuron or glial cell.

17. A method for reducing the level of Aβ secreted from a brain cell comprising contacting a mammalian brain cell with an agent that reduces expression or activity of a ABCA1 ATP-binding cassette protein.

18. The method of claim 17, wherein the agent is an agent that reduces ABCA1 protein activity.

19. The method of claim 18, wherein the agent binds to the ABCA1 protein.

20. The method of claim 19, wherein the agent is an antibody or an antibody fragment containing an antigen binding domain that binds to the ABCA1 protein.

21. The method of claim 18, wherein the agent is an antagonist of ABCA1 function.

22. The method of claim 17, wherein the agent is an agent that reduces ABCA1 protein expression.

23. The method of claim 22, wherein the agent is a molecule that induces RNA inhibition (RNAi).

24. The method of claim 22, wherein the agent is an antisense oligonucleotide.

25. The method of claim 22, wherein the agent reduces oxysterol and/or retinoic acid levels in the brain cell.

26. The method of claim 25, wherein the agent reduces oxysterol levels is a statin compound.

27. The method of claim 26, wherein the agent that reduces oxysterol levels is an inhibitor of a cytochrome P450 enzyme that generates oxysterols.

28. The method of claim 27, wherein the cytochrome P450 enzyme is CYP46 that makes 24-hydroxycholesterol.

29. The method of claim 22, wherein the agent is PPARδ modulator.

30. The method of claim 17, wherein said contacting occurs in vitro.

31. The method of claim 17, wherein the brain cell is a neuron or glial cell.

32. A method for modulating cholesterol efflux in a brain cell comprising

contacting a mammalian brain cell with an agent that reduces expression or activity of a liver X receptor (LXR) protein.

33. The method of claim 32, wherein the agent is an agent that reduces LXR protein activity.

34. The method of claim 33, wherein the agent binds to the LXR protein.

35. The method of claim 34, wherein the agent is an antibody or an antibody fragment containing an antigen binding domain that binds to LXR protein.

36. The method of claim 33, wherein the agent is an antagonist of LXR function.

37. The method of claim 36, wherein the LXR antagonist is geranylgeranyl pyrophosphate (GGPP).

38. The method of claim 32, wherein the agent is an agent that reduces LXR protein expression.

39. The method of claim 38, wherein the agent is a molecule that induces RNA inhibition (RNAi).

40. The method of claim 38, wherein the agent is an antisense oligonucleotide.

41. The method of claim 38, wherein the agent reduces oxysterol and/or retinoic acid levels in the brain cell.

42. The method of claim 41, wherein the agent reduces oxysterol levels is a statin compound.

43. The method of claim 42, wherein the agent that reduces oxysterol levels is an inhibitor of a cytochrome P450 enzyme that generates oxysterols.

44. The method of claim 43, wherein the cytochrome P450 enzyme is CYP46 that makes 24-hydroxycholesterol.

45. The method of claim 38, wherein the agent is PPARδ modulator.

46. The method of claim 32, wherein said contacting occurs in vitro.

47. The method of claim 32, wherein the brain cell is a neuron or glial cell.

48. A method for modulating cholesterol efflux in a brain cell comprising

contacting a mammalian brain cell with an agent that reduces expression or activity of a ABCA1 ATP-binding cassette protein.

49. The method of claim 48, wherein the agent is an agent that reduces ABCA1 protein activity.

50. The method of claim 49, wherein the agent binds to the ABCA1 protein.

51. The method of claim 50, wherein the agent is an antibody or an antibody fragment containing an antigen binding domain that binds to the ABCA1 protein.

52. The method of claim 49, wherein the agent is an antagonist of ABCA1 function.

53. The method of claim 48, wherein the agent is an agent that reduces ABCA1 protein expression.

54. The method of claim 53, wherein the agent is a molecule that induces RNA inhibition (RNAi).

55. The method of claim 53, wherein the agent is an antisense oligonucleotide.

56. The method of claim 53, wherein the agent reduces oxysterol and/or retinoic acid levels in the brain cell.

57. The method of claim 56, wherein the agent reduces oxysterol levels is a statin compound.

58. The method of claim 57, wherein the agent that reduces oxysterol levels is an inhibitor of a cytochrome P450 enzyme that generates oxysterols.

59. The method of claim 58, wherein the cytochrome P450 enzyme is CYP46 that makes 24-hydroxycholesterol.

60. The method of claim 53, wherein the agent is PPARδ modulator.

61. The method of claim 48, wherein said contacting occurs in vitro.

62. The method of claim 48, wherein the brain cell is a neuron or glial cell.

63. A method for reducing the rate of onset or the severity of Alzheimer's disease in a subject, comprising

administering to the subject an effective amount of one or more agents selected from the group consisting of: agents that decrease LXR expression or activity; and agents that decrease ABCA1 expression or activity.

64. The method of claim 63, wherein the agent administered is an agent that decreases LXR activity.

65. The method of claim 64, wherein the agent binds to the LXR protein.

66. The method of claim 65, wherein the agent is an antibody or an antibody fragment containing an antigen binding domain that binds to LXR protein.

67. The method of claim 64, wherein the agent is an antagonist of LXR function.

68. The method of claim 67, wherein the LXR antagonist is geranylgeranyl pyrophosphate (GGPP).

69. The method of claim 63, wherein the agent administered is an agent that decreases ABCA1 activity.

70. The method of claim 69, wherein the agent binds to the ABCA1 protein.

71. The method of claim 70, wherein the agent is an antibody or an antibody fragment containing an antigen binding domain that binds to the ABCA1 protein.

72. The method of claim 69, wherein the agent is an antagonist of ABCA1 function.

73. The method of claim 63, wherein the agent is an agent that reduces LXR or ABCA1 protein expression.

74. The method of claim 73, wherein the agent is a molecule that induces RNA inhibition (RNAi).

75. The method of claim 73, wherein the agent is an antisense oligonucleotide.

76. The method of claim 73, wherein the agent reduces oxysterol and/or retinoic acid levels in the brain cell.

77. The method of claim 76, wherein the agent that reduces oxysterol levels is a statin compound.

78. The method of claim 76, wherein the agent that reduces oxysterol levels is an inhibitor of a cytochrome P450 enzyme that generates oxysterols.

79. The method of claim 76, wherein the cytochrome P450 enzyme is CYP46 that makes 24-hydroxycholesterol.

80. The method of claim 73, wherein the agent is PPARδ modulator.

81. The method of claim 63, wherein the brain cell is a neuron or glial cell.

82. The method of claim 63, wherein the subject is a human.

83. The method of claim 63, further comprising to the subject an effective amount of a therapeutic agent for treating Alzheimer's disease selected from the group consisting of acetylcholine esterase inhibitors, beta- and gamma-secretase inhibitors, Abeta vaccines, Cu-Zn chelators, cholesterol-lowering drugs and non-steroidal anti-inflammatory drugs.

84. A composition for reducing Aβ secretion from a brain cell comprising

one or more agents that reduce LXR activity or expression and/or one or more agents that reduce ABCA1 activity or expression.

85. The composition of claim 84, further comprising a pharmaceutically acceptable carrier.

86. The composition of claim 84, further comprising a therapeutic agent for treating Alzheimer's disease.

87. The composition of claim 86, wherein the therapeutic agent for treating Alzheimer's disease is selected from the group consisting of acetylcholine esterase inhibitors, beta- and gamma-secretase inhibitors, Abeta vaccines, Cu-Zn chelators, cholesterol-lowering drugs and non-steroidal anti-inflammatory drugs.

88. The composition of claim 84, wherein the agent is an agent that decreases LXR activity.

89. The composition of claim 88, wherein the agent binds to the LXR protein.

90. The composition of claim 89, wherein the agent is an antibody or an antibody fragment containing an antigen binding domain that binds to LXR protein.

91. The composition of claim 88, wherein the agent is an antagonist of LXR function.

92. The composition of claim 84, wherein the agent administered is an agent that decreases ABCA1 activity.

93. The composition of claim 92, wherein the agent binds to the ABCA1 protein.

94. The composition of claim 93, wherein the agent is an antibody or an antibody fragment containing an antigen binding domain that binds to the ABCA1 protein.

95. The composition of claim 92, wherein the agent is an antagonist of ABCA1 function.

96. The composition of claim 84, wherein the agent is an agent that reduces LXR or ABCA1 protein expression.

97. The composition of claim 96, wherein the agent is a molecule that induces RNA inhibition (RNAi).

98. The composition of claim 96, wherein the agent is an antisense oligonucleotide.

99. The composition of claim 96, wherein the agent reduces oxysterol and/or retinoic acid levels in the brain cell.

100. The composition of claim 99, wherein the agent reduces oxysterol levels is a statin compound.

101. The composition of claim 96, wherein the agent is PPARδ modulator.

102. A kit comprising a composition of any of claim 84-101 and instructions for administering the composition to a subject having or suspected of having Alzheimer's disease.